



WITHANIA COAGULANS DUNAL- AN OVERVIEW

Prakash Chandra Gupta*

Department of Zoology, K. N. Government P. G. College, Gyanpur, S. R. N., Bhadohi, India.

*Corresponding author's E-mail: lightbhu@rediffmail.com

Accepted on: 09-11-2011; Finalized on: 20-01-2012.

ABSTRACT

In ancient system of medicine, many plants have been reported to cure various health problems and diseases. *Withania coagulans* (*W. coagulans*) Dual commonly known as 'Indian cheese maker' or 'vegetable rennet' belongs to family Solanaceae and is one of the important medicinal plants. *W. coagulans* Dunal is a gray-whitish small shrub distributed in east of the Mediterranean region extending to South Asia. It is a common medicinal plant in many parts of Pakistan and India. In Ayurvedic system of medicine, *W. coagulans* is widely used in diabetic cases. *W. coagulans* is also used to treat nervous exhaustion, disability, insomnia, wasting diseases, failure to thrive in children and impotence. The fruits of the plant are reported to be sedative, emetic, alterative and diuretic. Further, they are used for liver complaints, asthma and biliousness. The active compounds, in particular, withanolides isolated from the plant are considered to have antimicrobial, anti-inflammatory, antitumor, hepatoprotective, anti-hyperglycemic, cardiovascular, immuno-suppressive, free radical scavenging and central nervous system depressant activities. This review gives a bird's eye view mainly on the biological activities of some of the *W. coagulans* compounds isolated and phytochemistry as well as pharmacognostic properties of the plant extracts.

Keywords: Indian cheese maker, Anti-inflammatory, Withanolides, Cyclophosphamide.

INTRODUCTION

In ancient system of medicine, many plants have been reported to be useful to cure various health problems and diseases. Herbalism refers to traditional or folk medicine practice based on the use of plants and plant extracts. Charaka Samhita and Sushruta Samhita give extensive description on various medicinal plants. Medicinal plants play an important role in the development of new herbal drugs. Presently about 25% of pharmaceutical prescriptions in the United States contain at least one plant-derived ingredient¹. *Withania coagulans* (*W. coagulans*) Dual belongs to family Solanaceae and is one of the important medicinal plants. There are two species of *Withania*, viz., *W. somnifera* and *W. coagulans*, which are distributed in east of the Mediterranean region extending to South Asia. It is found in many parts of Pakistan and India². This plant carries different local names, such as 'Akri' or 'Puni-ke-bij' in Hindi, 'Tukhme-kaknaje-hindi' in Persian, 'Spiubajja in Afghan, 'Khamjira' in Panjabi and 'Punirband' or 'Punir-ja-fota' in Sindhi.

W. coagulans Dunal, is commonly known as 'Indian cheese maker' or 'vegetable rennet' because fruits and leaves of this plant are used as a coagulant. The milk coagulating property of the fruits is attributed to the pulp and husk berries which contain an enzyme called Withanin, having milk-coagulating activity. One ounce of the fruits of *W. coagulans* when mixed with 1 quart of boiling water makes a decoction, one table spoonful of which is capable to coagulate a gallon of milk in just an hour. In Pakistan, the berries of *W. coagulans* are commonly used to clot milk which is called, 'paneer'. The milk of buffalo or sheep is boiled to 100°F and treated

with crushed berries of the plant, tied in a cloth. This causes the milk to curdle within 30-40 minutes.



Withania coagulans plant



Withania coagulans fruits

The fruits of the plant are sweet and are reported to be sedative, emetic, alterative and diuretic. A composite Ayurvedic medicine 'Liv 52' is a hepatoprotective herbal preparation and contains extracts from *Withania coagulans* and *W. somnifera*. They are also used in dyspepsia, flatulent colic and other intestinal infections. In some parts of Pak-Indian sub-continent, the berries are used as a blood purifier. The twigs are often chewed for cleaning of teeth and the smoke of the plant is inhaled for relief in toothache^{3,4}. In addition, *W. coagulans* is used to treat nervous exhaustion, disability, insomnia, wasting diseases, failure to thrive in children, impotence. Its fruits are used for liver complaints, asthma and biliousness. Flowers of the plant are useful in the treatment of diabetes⁵. The root is harvested in autumn and dried for later use⁶. Some caution is advised in the use of the plant since it is toxic in nature⁷. This plant has been reported to possess antimicrobial, anti-inflammatory, antitumor, hepatoprotective, anti-hyperglycemic, cardiovascular, immuno-suppressive, free radical scavenging and central nervous system depressant activities⁸.

Botanical description

W. coagulans Dunal is a rigid, gray-whitish small shrub, about 60-120 cm tall. The leaves are about 2.5-7.5 cm long and 1.5 cm broad, usually lanceolate-oblong, sometimes ovate, obtuse, narrow at the base and very short stalked. The flowers are about 7-12 mm across, yellowish, and are dioecious and polygamous in nature. The flowers are found in axillary cymose clusters. The berries are about 7-12 mm in diameter, red, smooth and enclosed in leathery calyx. The seeds are dark brown, ear shaped, glabrous with sharp fruity smell.

Taxonomy:

Kingdom :	Plantae
Division :	Magnoliophyta
Class :	Magnolipsida
Order :	Solanales
Family :	Solanaceae
Genus :	<i>Withania</i>
Species :	<i>W. coagulans</i>

PHYTOCHEMICAL PROPERTIES

Aqueous and methanol extracts from the fruits of *W. coagulans* show a number of different phytoconstituents present in the plant which makes it remarkable for its use by traditional practitioners. Phytochemical screening of both the extracts showed the presence of alkaloids, steroids, phenolic compounds, tannins, saponins, carbohydrates, proteins, amino acids and organic acids⁹. A variety of withanolides (steroidal lactones) such as coagulin F [27-hydroxy-14,20-epoxy-1-oxo-(22R)-witha-3,5,24-trienolide], coagulin G [17beta,27-dihydroxy-14,20-epoxy-1-oxo-(22R)-witha-2,5,24-trienolide], coagulanolide (17S,20S,22R) [14alpha,15alpha,17beta,

20beta-tetrahydroxy-1-oxo-witha-2,5,24-trienolide], 20beta-hydroxy-1-oxo-(22R)-witha-2,5,24-trienolide and withacoagulin have been isolated from the whole plant of *W. coagulans*, and their structures have been elucidated and studied with the help of different spectroscopic techniques¹⁰⁻¹³. The phytochemical studies reported earlier indicate that the alkaloids and steroids isolated from plant sources are responsible for hypoglycemic activity of the plant.

PHARMACOGNOSTIC EFFECTS

Antihyperglycaemic and antihyperlipidemic effects

Aqueous and chloroform extracts prepared from *W. coagulans* fruits showed pharmacological effects on blood glucose, lipid profile and body weight in type 2 diabetic rats causing significant decrease in blood levels of glucose, triglyceride, total cholesterol, LDL and VLDL and an increase in HDL when administered alone or in combination once daily p.o., at a dose of 1 g/kg body weight for 14 days in different groups of normoglycemic and hyperglycemic rats^{14,15}. In addition, aqueous extract of fruits of the plant at the same dose significantly lowered serum LPO and hepatic LPO levels in streptozotocin induced diabetic rats as well as db/db mice^{16,17}. The dose of 1g/kg body weight was identified as the most effective dose of the plant extract to reduce Fasting Blood Glucose level maximum by 33.2 % at 4h in normal rats. On the other hand, Glucose Tolerance Test studies of normal, sub and mild diabetic rats showed the maximum reduction of 15.7, 28.9 and 37.8 % at 3h respectively confirming hypoglycemic and antidiabetic activities of aqueous extract of *W. coagulans*¹⁸.

Treatment with coagulanolide⁴ along with four known withanolides 1-3 and 5 isolated from *W. coagulans* fruits, showed significant inhibition on postprandial rise in hyperglycemia post-sucrose load in normoglycemic rats as well as streptozotocin-induced diabetic rats. The compound 5 also caused significant fall in fasting blood glucose profile and improved the glucose tolerance of db/db mice. Further, compound 5 showed antidyslipidemic activity in db/db mice. The median effective dose of the compound 5 was determined to be around 25 mg/kg body weight in streptozotocin-induced diabetic rats, which is comparable to the standard antidiabetic drug metformin. This explains the traditional use of *W. coagulans* as antihyperglycemic cum antidyslipidemic agent by the traditional medical practitioners¹⁹.

Wound healing activity

The hydroalcoholic fraction of the methanolic extract of *W. coagulans* was administered in the form of 10% w/w ointment topically and at a dose of 500 mg/kg body weight orally to streptozotocin-induced diabetic rats. The hydroalcoholic fraction in both the forms, i.e., topical (10% w/w ointment) and oral (500 mg/kg body weight, p.o.) showed a significant increase in the rate of wound contraction compared to diabetic controls²⁰.



Cardiovascular effects

A new withanolide, with a unique chemical structure similar to the aglycones of the cardiac glycosides (mol. wt. 488.6, m. p. 260-261 degrees), was isolated from the fruits of *W. coagulans*, and was screened for cardiovascular effects. At a dose of 5 mg/kg body weight, the withanolide produced a moderate fall of blood pressure in dogs (34 ± 2.1 , mm Hg) which was blocked by atropine and not by mepyramine or propranolol. In rabbit Langendorff preparation and ECG studies, it produced myocardial depressant effects; but in perfused frog's heart, it produced mild positive inotropic and chronotropic effects²¹.

Hepatoprotective effects

Protective effect of 3 β -hydroxy-2,3-dihydrowithanolide F isolated from *W. coagulans* was tested against CCl₄-induced hepatotoxicity, and the compound was found to possess marked protective effect. A comparison of the protective properties showed that it is more active than hydrocortisone on a weight basis²².

Immuno-suppressive effects

Six new withanolides, withacoagulins A-F (1-6, resp.), together with ten known withanolides, 7-16, were isolated from the aerial parts of *W. coagulans*. These compounds, including the crude extracts of this herb, exhibited strong inhibitory activities on the T- and B-cell proliferation²³.

Diuretic effect

The diuretic activity of the aqueous extract of fruits of *W. coagulans* was studied by *in vivo* Lipschitz test model with slight modifications using furosemide as a standard. The results indicated significant increase in the urine volume by 79.12 % and 71.02 % at 500 mg/kg and 750 mg/kg body weight doses respectively compared to controls. Urinary electrolyte excretions were increased at both the doses compared to controls²⁴.

Antimutagenic and anticarcinogenic effects

The genotoxic nature of any herbal drug is determined on the basis of presence of phytoconstituents. *W. coagulans* contains withanolides, which are reported for antitumor activity, and flavonoids which have been shown to possess antimutagenic and anticarcinogenic activities. The underlying mechanism behind anti-mutagenic action of *W. coagulans* is still unknown. The antimutagenic activity of *W. coagulans* fruit extracts was investigated on cyclophosphamide induced micronucleus formation in mouse bone marrow cells. The results confirmed that a single i.p administration of *W. coagulans* fruit extract at the doses of 500, 1000 and 1500 mg/kg body weight prior to 24 h significantly prevented the micronucleus formation in dose dependent manner in bone marrow cells of mice as compared to cyclophosphamide group²⁵.

Anti-inflammatory activity

Different extracts prepared from fruits of *W. coagulans* have been shown to possess anti-inflammatory properties²⁶.

Antifungal activity

Two new withanolides, 14,15 β -epoxywithanolide I [(20S,22R) 17 β ,20 β -dihydroxy-14 β ,15 β -epoxy-1-oxo-witha-3,5,24-trienolide] and 17 β -hydroxywithanolide K [(20S,22R) 14 α ,17 β ,20 β -trihydroxy-1-oxo-witha-2,5,24-trienolide], isolated from ethanolic extract of the whole plant of *W. coagulans*, have been found to be active against a number of potentially pathogenic fungi²⁷.

Antibacterial and antihelmintic activities

The volatile oil obtained from alcoholic extract of fruits of *W. coagulans* has antibacterial activity against *S. aureus* and *Vibrio cholera*, and it is also found to have antihelmintic activity^{28,29}.

CONCLUSION

Medicinal plants are part and parcel of human society to combat diseases from the dawn of civilization. *W. coagulans* has been found to contain a vast array of biologically active compounds, which are chemically diverse and have got an enormous therapeutic potential. Very little work has been done on the biological activity and plausible medicinal applications of the compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. Although crude extracts from various parts of *W. coagulans* particularly fruits have medicinal applications, modern drugs can be developed only after extensive investigation of their bioactivity, mechanism of action, pharmacotherapeutics, toxicity and after proper standardization and clinical trials.

REFERENCES

1. Anesini C and Perez C. Screening of plants used in Argentine folk medicine for antimicrobial activity. *J Ethnopharmacol*, 39: 1993, 119 – 128.
2. Chadha YR. The Wealth of India, Vol X, Publication and Information Directorate CSIR, New Delhi: 1976, pp. 580-85.
3. Dymock W, Waden C J H and Hopper D. *Pharmacographia Indica*, Institute of health and TB Research, Karachi: 1972, pp. 306.
4. Krishnamurthi A. The Wealth of India, Vol VIII, Publication Information Directorate, CSIR, New Delhi: 1969, pp.582.
5. Bown D. *Encyclopedia of Herbs and their uses*, Dorling Kindersley, London: 1995, pp. 500.
6. Chevallier A. *The Encyclopedia of medicinal plants*, Dorling Kindersley London: 1996, pp. 500.
7. Purohit S S and Vyas S P. *Medicinal plant cultivation: A Scientific approach*, Pub. Agrobios, Jodhpur: 2004, pp. 547.



8. Maurya J and Akanksha J. Chemistry and pharmacology of *Withania coagulans*: an Ayurvedic remedy. *Pharma Pharmacol*, 62: 2010, 153-160.
9. Mathur D, Agrawal R C and Shrivastava V. Phytochemical Screening and Determination of Antioxidant Potential of Fruits Extracts of *Withania coagulans*. *Recent Research in Science and Technology*, 3(11): 2011, 26-29.
10. Atta-ur-Rahman A, Choudhary M I, Qureshi S, Gul W and Yousaf M. Two new ergostane-type steroidal lactones from *Withania coagulans*. *J Nat Prod*. 61(6): 1998, 812-814.
11. Atta-ur-Rahman, Shabbir M, Yousaf M, Qureshi S, Dur-e-Shahwar, Naz A and Choudhary M I. Three withanolides from *Withania coagulans*. *Phytochemistry*, 52(7): 1999, 1361-1364.
12. Atta-ur-Rahman A, Dur-e-Shahwar, Naz A and Choudhary M I. Withanolides from *Withania coagulans*. *Phytochemistry*. 63(4): 2003, 387-390.
13. Ramaiah P A, Lavie D, Budhiraja R D, Sudhir S and Garg K N. Spectroscopic studies on a withanolide from *Withania coagulans*. *Phytochemistry*, 23(1): 1984, 143-149.
14. Hoda Q, Ahmad S, Akhtar M, Najmi A K, Pillai K K and Ahmad S J. Antihyperglycaemic and antihyperlipidemic effects of poly-constituents, in aqueous and chloroform extracts, of *Withania coagulans* Dunal in experimental type 2 diabetes mellitus in rats. *Hum Exp Toxicol*. 29(8): 2010, 653-658.
15. Hemalatha S, Wahi A K, Singh P N and Chansouria J P. Hypolipidemic activity of aqueous extract of *Withania coagulans* Dunal in albino rats. *Phytother Res.*, 20(7): 2006, 614-617.
16. Hemalatha S, Wahi A K, Singh P N and Chansouria J P. Hypoglycemic activity of *Withania coagulans* Dunal in streptozotocin induced diabetic rats. *J Ethnopharmacol*. 93(2-3): 2004, 261-264.
17. Bhudhiraja R D, Sudhir S and Garga K N. Pharmacological investigations on fruits of *Withania coagulans* Dunal. *Planta Med* 32: 1977, 154-157.
18. Jaiswal D, Rai P K and Watal G. Antidiabetic effect of *Withania coagulans* in experimental rats. *Indian Journal of Clinical Biochemistry*, 24 (1): 2009, 88-93.
19. Maurya R, Akanksha, Jayendra, Singh A B and Srivastava A K. Coagulanolide, a withanolide from *Withania coagulans* fruits and antihyperglycemic activity. *Bioorg Med Chem Lett*. 18(24): 2008, 6534-6537.
20. Prasad S K, Kumar R, Patel D K and Hemalatha S. Wound healing activity of *Withania coagulans* in streptozotocin-induced diabetic rats. *Pharm Biol*. 48(12): 2010, 1397-1404.
21. Budhiraja R D, Sudhir S and Garg K N. Cardiovascular effects of a withanolide from *Withania coagulans* Dunal fruits. *Indian J Physiol Pharmacol*. 27(2): 1983, 129-134.
22. Budhiraja R D, Bala S, Craeg F N and Arora B. Protective effect of 3-beta-hydroxy-2-3 dihydro withanolide-F against CCl₄ induced Hepatotoxicity. *Planta Medica*, 52(1): 1986, 28-29.
23. Huang C F, Ma L, Sun L J, Ali M, Arfan M, Liu J W and Hu L H. Immunosuppressive withanolides from *Withania coagulans*. *Chem Biodivers*. 6(9): 2009, 1415-1426.
24. Dabheriya J, Khan S A, Joshipura M, Vasoya M, Patel S and Vijaya S. Diuretic poteial of aqueous extract of fruits of *Withania coagulans* Dunal in experimental rats. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2(4): 2010, 51-53.
25. Mathur D and Agrawal R C. Evaluation of *in vivo* antimutagenic potential of fruits extracts of *Withania coagulans*. *Der Pharma Chemica*, 3 (4): 2011, 373-376.
26. Rajurkar S M, Thakre P N and Waddukar S G. Phytochemical and pharmacological screening of *Withania coagulans* berries as anti-inflammatory. *Sci Abst CP38*, New Delhi: 2001, pp. 215.
27. Choudhary M I, Dur-e-Shahwar, Zeba P, Jabbar A, Ali I and Rehman A. Antifungal steroidal lactones from *W. coagulans*. *Phytochemistry*, 40(4): 1995, 1243-1246.
28. Khan M T J, Ashraf M, Tehniyat S, Bukhtair M K, Ashraf S and Ahmed W. Anti bacterial activity of *W. coagulans*. *Fitoterapia*, 64: 1993, 367-378.
29. Gaind K N and Budhiraja R D. Antibacterial and antihelmintic activity of *Withania coagulans* Dunal. *Indian J Pharmacol*, 29: 1967, 185-186.

